



PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61K 38/55</b>		A3	(11) International Publication Number: <b>WO 97/34627</b> (43) International Publication Date: 25 September 1997 (25.09.97)
(21) International Application Number: <b>PCT/IB97/00499</b> (22) International Filing Date: 19 March 1997 (19.03.97) (30) Priority Data: 08/616,489 19 March 1996 (19.03.96) US (60) Parent Application or Grant (63) Related by Continuation US 08/616,489 (CON) Filed on 19 March 1996 (19.03.96) (71) Applicants (for all designated States except US): SOCIETE DE CONSEILS DE RECHERCHES ET D'APPLICATIONS SCIENTIFIQUES S.A. (FR/FR); 51-53, rue du Docteur- Blanche, F-75016 Paris (FR). INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (FR/FR); 101, rue de Tolbiac, F-75654 Paris Cédex 13 (FR). (72) Inventors; and (75) Inventors/Applicants (for US only): WDZIECZAK-BAKALA, Joanna (FR/FR); 9, avenue de Saint-Mande, F-75012 Paris (FR). ROUSSEAU-PLASSE, Anne (FR/FR); 18, rue Pottier,		F-78150 Les Chesnay (FR). LENFANT, Maryse (FR/FR); 18, rue des Chataigniers, F-91190 Gif-sur-Yvette (FR). (74) Agent: COCKBAIN, Julian; Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL (GB). (81) Designated States: CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published With international search report. (88) Date of publication of the International search report: 18 December 1997 (18.12.97)	
(54) Title: PROTECTION OF HEMOPOIETIC CELLS DURING CHEMOTHERAPY OR RADIOTHERAPY			
(57) Abstract  A method of promoting regeneration of hemopoietic cells in a subject undergoing chemotherapy or radiotherapy, which method includes administering to the subject an angiotensin-converting enzyme inhibitor, the amount being effective to reduce the proliferation of hemopoietic cells during or after said chemotherapy or radiotherapy.			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BI	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

# INTERNATIONAL SEARCH REPORT

Intern. Appl. No.

PCT/IB 97/00499

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K38/55

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AZIZI M ET AL: "Acute angiotensin-converting enzyme inhibition increases the plasma level of the natural stem cell regulator N-acetyl-seryl-aspartyl-lysyl-proline" JOURNAL OF CLINICAL INVESTIGATION, 97 (3). 1996. 839-844., XP002042150 see page 843, column 1, paragraph 23	1-24
Y	RIEGER K-J ET AL: "Involvement of human plasma angiotensin I-converting enzyme in the degradation of the haemoregulatory peptide N-acetyl-seryl-aspartyl-lysyl-proline" BIOCHEMICAL JOURNAL, 296 (2). 1993. 373-378., XP002042151 see page 377, column 1, paragraph 4 - page 378, column 2, paragraph 1	1-24

-/--

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"B" document member of the same patent family

Date of the actual completion of the international search

30 September 1997

Date of mailing of the international search report

17.10.1997

Name and mailing address of the ISA

European Patent Office, P. B. 5818 Patentkan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl  
Fax: (+31-70) 340-3016

Authorized officer

Leherte, C

# INTERNATIONAL SEARCH REPORT

Inter. Appl. Application No.

PCT/IB 97/00499

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MOORE M A S ET AL: "SYNERGY OF INTERLEUKIN 1 AND GRANULOCYTE COLONY-STIMULATING FACTOR IN-VIVO STIMULATION OF STEM-CELL RECOVERY AND HEMATOPOIETIC REGENERATION FOLLOWING 5 FLUOROURACIL TREATMENT OF MICE" PROC NATL ACAD SCI U S A, 84 (20). 1987. 7134-7138., XP002042152 see abstract ---	1-24
Y	ROUSSEAU A ET AL: "The hemoregulatory peptide N-acetyl-Ser-Asp-Lys-Pro is a natural and specific substrate of the N-terminal active site of human angiotensin-converting enzyme" JOURNAL OF BIOLOGICAL CHEMISTRY, 270 (8). 1995. 3656-3661., XP002042153 see page 3660, column 2, paragraph 2 ---	1-24
Y	US 5 114 926 A (FRINDEL EMILIA ET AL) 19 May 1992 see claims 2,9,10 ---	1-24
A	MOULDER, JOHN E. ET AL: "Prophylaxis of bone marrow transplant nephropathy with captopril, an inhibitor of angiotensin-converting enzyme" RADIAT. RES., 1993, 136, 404-7, XP002042154 see page 406, column 1 - page 407, column 1 ----- 0	1,24

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 97/00499

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 1-24  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Appl. Application No

PCT/IB 97/00499

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5114926 A	19-05-92	AU 598897 B	05-07-90
		FR 2601678 A	22-01-88
		NO 175102 B	24-05-94
		NO 173655 C	12-01-94
		AU 1026188 A	27-07-89
		CA 1337731 A	12-12-95
		DE 3781691 A	15-10-92
		EP 0316322 A	24-05-89
		WO 8800594 A	28-01-88
		JP 2500269 T	01-02-90
		JP 2542407 B	09-10-96
-----			